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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/759,360	01/16/2001	Wolfgang Halfbrodt	SCH-1738	1922

7590 10/06/2004

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EXAMINER	
ROBINSON, BINTA M	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 10/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/759,360	HALFBRODT ET AL.	
	Examiner	Art Unit	
	Binta M Robinson	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-24,26,29,30,32-38,40 and 42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-24,26,29,30,32-38,40 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

The 112, first paragraph rejection of claims 1-42, the 112, second paragraph rejections of claims 1-42 and the 102 (b) rejections of claims 1-40 made in the office action mailed 3/23/04, are withdrawn as a result of applicant's amendments and remarks in the amendment filed 9/17/04. The restriction requirement is modified so that the elected subject is drawn to the method for treating a patient with the compound of formula II as defined in the claims filed 6/30/04

(new rejections)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15-24, 26, 29, 30, 32, 33, 34, 35, 36, 37, 38, 40, 42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement for a method of treating a patient suffering from chronic inflammation or a disease associated with chronic inflammation with the instant compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is

"undue". These factors include 1)the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art 6) the amount of direction provided by the inventor 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In terms of factor 3 and 5, the state of the art and the level of predictability in the art cannot be predicted with any certainty beyond what specific test compounds /compositions and/or additional therapeutic agents should be used and are likely to provide productive results beyond those therapeutic compounds/compositions and/or additional therapeutic agents taught in the specification. There is no indication which compounds where tested for their effect on microglial activation.

The nature of the invention

The nature of the invention is the synthesis of novel benzimidazole compounds and their use in the treatment and prophylaxis of chronic inflammation and diseases associated with chronic inflammation.

The state of the prior art

The state of the prior art is that a central step of the inflammation process is the activation of microglia. This is carried out in diseases such as Alzheimer's disease. The microglia can remain for a prolonged period in the activated state, in which they produce and secrete various inflammation factors. These factors produce

neuronal dysfunction and degeneration. Treatment of neuroinflammation to date has been with steroidal anti-inflammatory agents see page 1 of the specification, cytokine modulators, page 2 of the specification, and complement-cascade-inhibitors, see page 2 of the specification. These substances inhibit the syntheses or the action of individual inflammation factors. However, the claimed invention sets out to inhibit an earlier step in the inflammation process and thus prevent the development of any inflammatory factors. Minocycline has been shown to block microglial activation of 6-hydroxydopamine and 1-methyl-4-phenyl-1,2,3-6-tetrahydropyridine-lesioned parkinsonism animal models. See abstract on page 679 of Thomas et. al. However, no clinical trials published to the date of the publication of the Thomas et. al., article have been conducted on the use of MC for the management of Parkinson's disease. See page 684, of Thomas et. al. However, inhibitors of microglial activation have not been known in the art to treat chronic inflammation itself or diseases or Parkinson's disease that are associated with chronic inflammation.

The predictability or lack thereof in the art

The instant claimed invention is highly unpredictable as discussed below:
In the instant case, the claimed invention is highly unpredictable because of the absence of the claiming of the actual diseases that are said to be associated with microglial activation. The applicant has not shown that by inhibiting microglial activation, that specific diseases are being treated. The applicant has not claimed which diseases are actually being treated by inhibiting microglial activation. The nature of this art is that it involves screening in vitro and in vivo

to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The amount of direction or guidance present

The direction present in the instant specification is that the instant compounds can inhibit microglial activation which helps in the treatment of diseases such as Alzheimer's which is said to be mediated by microglial activation. However, the specification is silent and fails to provide a correlation between the diseases listed in the specification and the inhibition of microglial activation. The specification fails to provide any experimental data of the effect of these compounds on microglial activation and specific diseases correlated with microglial activation.

The presence or absence of working examples

The applicant provides no working examples for the treatment of diseases association with microglial activation. Also, the compounds, which are disclosed in the specification, have no pharmacological data regarding the treatment of any disease. Also, the specification fails to provide working examples as to how the diseases associated with microglial activation in the specification can be treated by inhibition of microglial activation.

The breadth of the claims

The breadth of the claims is that the compound of claim 15 can treat any disease associated with microglial activation.

The quantify of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what specific diseases would be benefited by the inhibition of microglial activation and would furthermore then have to determine whether the claimed compounds would provide treatment of the disease by the inhibition of microglial activation.

The level of skill in the art

The level of skill in the art is high. However, due to the unpredictability in the art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of claim 1 for the treatment of an NO-mediated disease. As a result, necessitating one of skill to perform an exhaustive search for which NO-mediated diseases can be treated by the compound of claim 1 in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its

successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which microglial activation associated diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

Working examples

There is no indication which compounds where tested for their effect on microglial activation. An indeterminate quantity of experimentation would be necessary to determine all potential therapeutic compounds/compositions' effects on microglia activation.

Quantity of experimentation

In terms of the 8th Wands factors, undue experimentation would be required to use the invention based on the content of the disclosure due to the breadth of the claims, the level of predictability in the art of the invention, and the poor amount of direction provided by the inventor. Taking the above factors into consideration, it is not seen where the instant claim is enabled by the instant application.

As a result one of ordinary skill in the art could not predict what other types of therapeutic compounds/compositions and/or additional therapeutic agents, other than

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703)308-4242, (703)305-3592, and (703)305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)-272-1600.

BMR
October 1, 2004

Cecilia J. Tsang
Supervisory Patent Examiner
Technology Center 1600